# Hepatitis C infection among injecting drug users in general practice: a cluster randomised controlled trial of clinical guidelines' implementation

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## ABSTRACT

### Background

Hepatitis C is a common infection among injecting drug users and has important implications for general practice. Although several clinical guidelines concerning the infection have been published, their effectiveness has yet to be tested.

### Aim

To assess the effectiveness of a general practice-based complex intervention to support the implementation of clinical guidelines for hepatitis C management among current or former drug users attending general practice.

### Design of study

Cluster randomised controlled trial.

### Setting

General practices in the Eastern Regional Health Authority area of Ireland.

### Method

Twenty-six practices were randomly allocated within strata to receive the intervention under study or to provide care as usual for a period of 6 months. There was screening for patients attending general practice for methadone maintenance treatment for hepatitis C and referral of anti-HCV antibody positive patients to a specialist hepatology department for assessment.

### Results

At study completion, patients in the intervention group were significantly more likely to have been screened for hepatitis C than those in the control group, odds ratio adjusted for clustering 3.76 (95% confidence interval [CI] = 1.3 to 11.3) and this association remained significant after adjusting for other potentially confounding variables, using multiple logistic regression, with the odds ratio adjusted for clustering 4.53 (95% CI = 1.39 to 14.78). Although anti-HCV antibody positive patients in the intervention group were more likely to have been referred to a hepatology clinic, this was not statistically significant ($P$ = 0.06).

### Conclusion

General practice has an important role in the care of people at risk of hepatitis C and when appropriately supported can effectively implement current best practice.

### keywords

clinical trial; cluster analysis; family practice; guidelines; hepatitis C; randomised controlled trial; screening.

## INTRODUCTION

Hepatitis C infection is a common infection worldwide.[1] In the UK, injecting drugs is a risk factor in the majority of infections[2] and in Ireland, 62–81% of injecting drug users have been reported to test positive for hepatitis C.[3,5]

The high prevalence of hepatitis C among this patient group has clear implications for general practice, whose role in caring for current or former injecting drug users in Ireland, the UK and other EU countries is established.[6,8] Specifically, its potential role in preventing new infections through engaging patients in harm reduction interventions, screening patients at risk of infection and providing diagnostic and therapeutic interventions to those who test positive has been recently highlighted.[9,10]

However, ensuring comprehensive and effective hepatitis C screening and care is a challenge for general practice in Ireland. A recent audit of blood borne virus care among current or former drug users attending general practice for treatment in the greater Dublin area, reported 34% had been screened for hepatitis C infection in general practice.[4]

In recent years, several clinical guidelines on hepatitis C care have been published.[11,14] At the time

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of this study, while the effectiveness of clinical guidelines in improving management of hepatitis C in general practice had not been demonstrated, an emerging consensus existed that successful guideline implementation in general practice required adopting multi-faceted interventions addressing potential barriers to change.[15,16]

We aimed to assess the effectiveness of a complex intervention, involving the dissemination of clinical guidelines and the provision of an accompanying implementation programme targeting multiple barriers to change, to improve hepatitis C care among current or former drug users attending general practice for methadone maintenance treatment, in a cluster randomised controlled trial.

## How this fits in

Injecting drugs is the main route of transmission of the hepatitis C virus in the UK and Ireland. This has important implications for general practice whose role in the treatment of people who have injected drugs is established. A cluster randomised controlled trial of a complex intervention to implement recently published clinical guidelines, designed after consultation with local GPs, demonstrated that the dissemination of clinical guidelines plus clinical and educational support resulted in measurable improvements in screening for hepatitis C infection and several other aspects of patient care.

## METHOD

### Setting and context

Since the introduction of legislation regulating the prescribing and dispensing of methadone in Ireland, it is not possible for doctors to prescribe nor for pharmacists to dispense methadone unless a patient's name has been entered on the 'Central Methadone Treatment List', a database of patients on methadone treatment coordinated by the Department of Health and Children.[20] To prescribe methadone, GPs are subject to clinical audit and must complete special training, with GPs providing methadone treatment for 15 or more patients subject to more regular audit and advanced training. GPs who prescribe methadone for less than 15 patients are referred to as 'level one GPs,' and those prescribing for 15 or more as 'level two' GPs. Initiation of methadone therapy is only permitted by specialist addiction treatment services or by 'level two' GPs.[20] This system is analogous to the GPs with a special interest model currently operating in the UK.[6]

### Intervention

Clinical guidelines for the management of hepatitis C were developed by a multidisciplinary expert panel. Content was derived from scientific evidence where this was available and from a Delphi-facilitated consensus development process where it was not and included: general advice on lifestyle, immunisation against other hepatotrophic viruses, screening for hepatitis C (and other bloodborne viruses), subsequent diagnosis (including polymerase chain reaction (PCR) testing and addiction–related care) and specialist assessment. The development and content of these guidelines have been reported separately.[21]

The intervention was developed subsequent to a series of semi-structured interviews with a sample of GPs currently involved in providing methadone maintenance treatment in the region. It consisted of disseminating the clinical guidelines practice based educational sessions that covered guidelines' content and their implementation and nursing support.[22] Nursing support consisted of a liaison nurse who was responsible for discussing the content of the guidelines with all practice staff (both clinical and non-clinical), identifying the needs of each practice with regard to effective implementation of the guidelines, providing clinical and administrative support to individual practices, training practice nursing and other staff, providing advice and support to practice nurses and GPs, encouraging the uptake of the clinical guidelines and liaising with specialist hepatology and addiction treatment services. The liaison nurse held a 1.0 whole–time equivalent post for the duration of the study.

Consultations held by the liaison nurse with individual patients were consistent with the clinical guidelines' content and included counselling and screening patients for infection with hepatitis C and other bloodborne viruses, immunising patients against other hepatotrophic viruses, counselling patients on the implications of testing positive for hepatitis C on initial screening and facilitating subsequent investigations among those identified as hepatitis C-positive. GPs in participating practices remained clinically responsible for individual patient care throughout the intervention period.

The intervention lasted for 6 months. This was felt to be of sufficient duration for significant outcomes to be detected and sufficiently short to avoid contamination by other initiatives.

### Study outcomes

Two outcomes, screening at risk populations for hepatitis C infection and antiviral therapy were considered as primary outcomes for the study, as both were associated with improved clinical outcomes and are cost-effective.[23–28] However, at the time of this study, it was not possible, nor did the clinical guidelines recommend, that antiviral therapy be initiated in general practice. For these reasons,

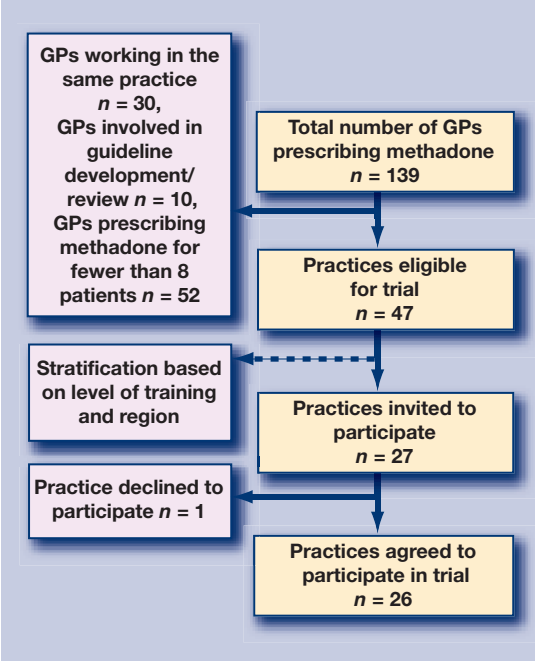



*Figure 1. Recruitment of practices for the trial.*

the primary outcomes were the proportion of current or former drug users attending general practice for methadone treatment who had been screened for hepatitis C infection and the proportion of anti-hepatitis C antibody positive patients who had been referred to a specialist hepatology department for assessment regarding treatment.

### Sample size considerations

Recent data on blood-borne virus care among drug users attending general practice for methadone maintenance treatment in the ERHA area estimated that only 34% of all patients that had been screened for hepatitis C infection in general practice and only 35% of those known to be hepatitis C-positive had been referred to a hepatologist for assessment.[4,29]

To detect a twofold increase in levels of hepatitis C screening and a twofold increase in the proportion of hepatitis C-positive patients who had been referred to a specialist for assessment, it was estimated that data on 156 and 201 patients, respectively, would be needed. This assumed a power of 80%, a confidence level (CI) of 95%, hepatitis C prevalence of 73%[4] and an intracluster correlation coefficient (ICC) of 0.15 (which in the absence of data estimating the ICC for hepatitis C care, was felt to be a conservative upper limit).[30]

To maximise the number of practices eligible for recruitment, thus minimising the design effect, and to ensure efficient use of resources in delivering the complex intervention, a pragmatic decision to adopt a cluster size of eight patients per practice was selected. Hence, data was required on each of the eight patients attending 27 practices.

### Recruitment and allocation of practices

Practices were eligible for inclusion in the study if one of the GP principals was registered to prescribe methadone and at least eight patients were currently being prescribed methadone in the practice and excluded if one of the GP principals had been involved in developing or reviewing the guidelines. In addition, practices where more than one GP was registered to prescribe methadone were considered as one practice for the purpose of the study, leaving a total of 47 practices eligible to participate (Figure 1).

A stratified random sampling technique (based on level of training of the GP principals and area of practice) was used to select 27 practices out of the 47 eligible, of which 26 practices (prescribing methadone to 538 patients) agreed to participate in the study.

To ensure comparability between intervention and control groups, practices were stratified according to the level of training of the GP principals in providing addiction care and according to whether their practice employed a practice nurse. Following stratification, a restricted randomisation procedure was carried out, whereby practices in each stratum were assigned a number and random numbers used to select practices that would comprise the control group, with the remainder being allocated to the intervention group.

Of the 26 practices randomised, 25 recruited patients for the trial (13 in the intervention group and 12 in the control group). One practice withdrew after randomisation from the control group, owing to practice restructuring.

A staggered intervention design was adopted, whereby practices randomised to the intervention arm of the trial were provided with the complex intervention for the duration of the study period, with the practices randomised to the control arm of the trial providing usual care to patients for the duration of the study and provided with the complex intervention thereafter.

### Recruitment of patients

The systematic and consistent random sampling of patients in the participating practices was not guaranteed and hence, a standardised non-probability sampling framework was used to identify eight patients from each practice on whom data would be collected for the purpose of the study. GPs in participating practices provided consecutive patients requesting a prescription for methadone with written information on the project and subsequently asked each patient to consent to allow a member of the research team have access to their medical records.

### Data collection

The clinical record of each consenting patient was

examined on-site by one of the research team, who had no input into clinical care or into the implementation of guidelines. The accuracy of data extraction was checked by the principal investigator who examined 10% of the records at baseline and on study completion.

Data were collected at time zero and after 6 months and included the primary outcome measures (evidence of screening for hepatitis C in the practice and of referral of hepatitis C-positive patients to a hepatology department), demographic and drug using characteristics and all aspects of clinical care covered by the clinical guidelines including: general aspects of care, screening for other blood borne viruses, immunisation against other hepatotrophic viruses, and subsequent management of hepatitis C-positive patients.

At the time of the study, GPs were required to monitor compliance and use of illicit drugs among patients on methadone maintenance treatment by testing urine samples for methadone, morphine, amphetamine, cocaine and benzodiazepine metabolites at intervals of no more than a week. The results of urinalysis testing for each patient during the previous 3 months were reviewed and the number of samples containing metabolites of non-prescribed illicit drugs was recorded.

Evidence of patients being screened for blood borne virus infections was based on the presence of results of anti-HCV antibody, anti-HIV antibody, HBSag or anti-HBc antibody testing in individual patient records held by the practice. At the time of the study, testing for hepatitis C antibodies (anti-HCV antibody) was with a third generation enzyme linked immunoadsorbent assay (EIA), with positive assays confirmed by radioimmunoblot (RIBA) assay; testing for HIV antibodies (anti-HIV) involved two EIAs, with positive assays confirmed by Western Blot assay and testing for both HBV surface antigen (HBSag) and HBV core antibody (anti-HBc) was with an EIA.

### *Data analysis*

Analysis of primary outcomes was by intention to treat and was performed in three steps with the least conservative described first.

The proportions of patients in intervention and control populations who had been screened for anti-hepatitis C antibody by their GP and if positive, to have been referred to or attended a specialist hepatology clinic for assessment were compared using the Mantel-Haenszel pooled odds ratio.

Using the 'svyset' series of commands in STATA version 6.0, logistic regression analysis (using 'svylogit') was performed to allow for the potential bias introduced by the clustered design. In this analysis, the practice variables used in the stratified

**Table 1. Participating GPs compared with all GPs providing methadone maintenance treatment in the region.**

| Variable | Characteristic | Participating GPs (*n* = 25) | All GPs (*n* = 139) |
|---|---|---|---|
| Patients on methadone | <15 | 11 | 95 |
| | >15 | 14 | 44 |
| Level of training | | | |
| Basic | ('level one') | 18 | 110 |
| Advanced | ('level two') | 7 | 29 |
| Health board area | | | |
| A | | 12 | 6 |
| B | | 10 | 45 |
| C | | 3 | 26 |

**Table 2. Baseline comparison of intervention and control groups at cluster and individual levels.**

| Characteristic | Intervention | Control |
|---|---|---|
| Practice factors at baseline | (*n* = 13) | (*n* = 12) |
| Area of practice | | |
| A | 5 | 7 |
| B | 7 | 3 |
| C | 1 | 2 |
| Single practitioner | | |
| Yes | 6 | 6 |
| No | 7 | 6 |
| Number of patients on methadone | | |
| <15 | 6 | 5 |
| ≥15 | 7 | 7 |
| Type of clinical record | | |
| Paper | 3 | 4 |
| Electronic | 1 | 2 |
| Combination | 9 | 6 |
| Preferred hepatology unit for referral | | |
| D | 5 | 7 |
| E | 1 | 2 |
| F | 4 | 2 |
| G | 3 | 1 |
| Patient factors at baseline | (*n* = 104) | (*n* = 92) |
| Mean age (years) | 33.1 | 31.8 |
| Mean time attending practice for methadone treatment (months) | 33.2 | 27.8 |
| Mean age of first using drugs (years) | 17.1 | 16.9 |
| Mean age of first injecting (years) | 20.0 | 19.9 |
| Male, *n* (%) | 84/104 (81) | 58/92 (63) |
| Provided urine sample containing metabolite of any illicit drug in the previous 3 months (%) | 57/104 (55) | 42/92 (46) |
| Provided urine sample containing opiate metabolite in the previous 3 months (%) | 35/104 (34) | 25/92 (27) |
| Screened for hepatitis C by GP (%) | 35/104 (34) | 24/92 (26) |
| Referral initiated if HCV antibody positive (%) | 20/67 (30) | 11/37 (30) |
| Attended specialist clinic if HCV antibody positive (%) | 16/67 (24) | 8/37 (22) |

randomisation process, namely the presence of a practice nurse and the level of training in providing addiction related care of the GP were included as 'strata', practices were included as the primary sampling units ('PSUs') and individual patients were assigned a weighting based on the inverse probability of that patient being selected from all patients attending that practice ('pweight').

To allow for potentially confounding variables that had not been considered in this stratification process, further logistic regression analysis was performed on the clustered dataset.

We considered *P* values of <0.05 and of <0.01 to imply statistical significance in the case of primary and secondary outcomes respectively.

## RESULTS

### Baseline data

The sample of GPs participating in the study was representative of all GPs in the region prescribing methadone in terms of the level of training in providing addiction care and the health board area in which their practice was located, but had a higher proportion of GPs providing methadone maintenance treatment to 15 or more patients (Table 1). Compared to a national census of GPs, the sample had a lower proportion of female GPs, a higher proportion of GPs with personal GMS lists and a higher proportion of GPs working in a practice that employed a practice nurse.[31,32]

There were no differences between the 'intervention' and 'control' practices for a range of characteristics, including: health board area of practice, type of clinical record used, number of patients on methadone maintenance treatment, and whether the practice consisted of a single GP (Table 2).

Patients attending 'intervention' and 'control' practices were comparable in terms of demography, drug using history, recent illicit drug use, screening for hepatitis C and referral to and attendance at a specialist unit for assessment if HCV antibody positive. The 'intervention' group of patients contained a significantly higher proportion of males compared to the control (Table 2).

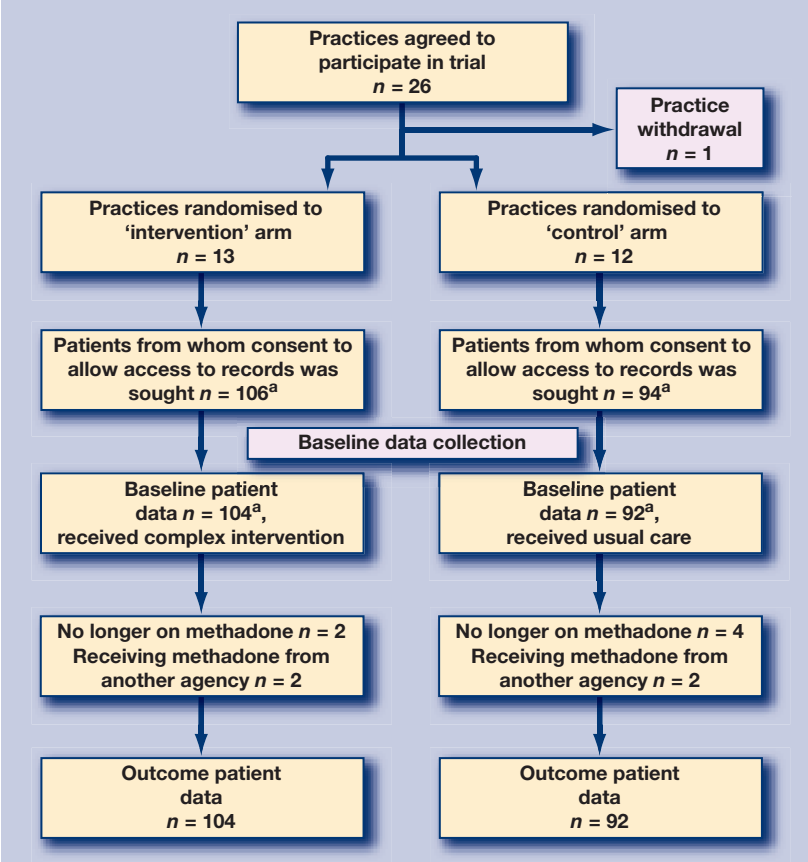
### Participant flow and follow up

Figure 2 illustrates the flow and follow up of patients through the trial. Although all practices had at least eight patients on methadone maintenance treatment at recruitment, at the time baseline data were collected, one practice had only six and two practices had only seven patients on methadone maintenance treatment. Therefore, data were recorded on 196 patients attending 25 practices, with 104 attending 'intervention' and 92 attending 'control' practices.

Although 11 patients were no longer receiving methadone maintenance treatment from their GP at follow up (6% of total), all 11 were still registered as continuing to attend the practice for general medical care and in this regard, were not considered as losses to follow up. For this reason and because analysis of outcome data is presented on an intention to treat basis, these cases were included in subsequent analyses.

There were no significant differences between groups for the proportions of patients no longer being prescribed methadone, who had stopped methadone treatment or who were being prescribed methadone by another agency. Five of the 104 patients in the 'intervention' arm of the trial were no longer receiving methadone maintenance treatment from their GP at trial completion. Of these, two were no longer on methadone treatment and three were being prescribed methadone by another agency. Six of the 92 patients in the 'control' arm of the trial were no longer receiving methadone maintenance treatment from their GP at trial completion. Of these, four were no longer on methadone treatment and two were being prescribed methadone by another agency.

***Figure 2. Consort diagram representing follow up of patients through the trial.***




[a]*Although all practices had at least eight patients on methadone treatment at recruitment, at baseline data collection, two practices had only seven patients and one practice had only six patients.*

**Table 3. Comparison of primary outcome measures between intervention and control populations at study completion analysed at patient and cluster level.**

| Evidence of primary outcome in clinical record | Intervention *n* (%) | Control *n* (%) | Odds ratio[a] (95% CI) | Adjusted odds ratio[b] (95% CI) | *P*-value | ICC (95% CI) |
|---|---|---|---|---|---|---|
| Screened for hepatitis C by GP | 51/104 (49) | 25/92 (27) | 2.58 (1.4-4.7) | 3.76 (1.3-11.3) | 0.02 | 0.09 (0.0-0.3) |
| Referral initiated if HCV antibody positive | 44/73 (60) | 13/41 (32) | 3.27 (1.5-7.3) | 3.15 (0.9-10.7) | 0.06 | 0.13 (0.0-0.5) |

[a]*Patient level analysis.* [b]*Cluster level analysis. ICC = intracluster correlation coefficient.*

No deaths were reported in either intervention or control populations during the study period.

### *Primary outcomes*

At study completion, patients in the intervention group were significantly more likely to have been screened for hepatitis C in general practice than those in the control group and if anti-HCV antibody positive were significantly more likely to have been referred to a hepatology clinic for assessment. However, after correction for clustering, only the former remained statistically significant (Table 3).

Further logistic regression analysis was performed in which potentially confounding variables not considered in the stratification process, were entered into a logistic regression equation against whether patients had been screened for hepatitis C. These variables included: if the practice had one doctor, had less than 15 patients on methadone maintenance, the health board area in which the practice was located, the type of clinical records used in the practice, patient gender and the preferred hepatology unit for referral. On this analysis, being in the intervention group was the only variable significantly associated with having been screened for hepatitis C in general practice, odds ratio = 4.53; 95% CI = 1.39 to 14.78; $P = 0.02$.

The intracluster correlation coefficients (95% CI) for the primary outcomes were 0.09 (0.00 to 0.33) in respect of screening for hepatitis C in general practice and 0.13 (0.00 to 0.50) in respect of referral of anti-HCV antibody positive patients to a hepatology unit, findings consistent with the ICC used to determine sample size.

### *Secondary outcomes*

After correction for clustering, patients in the intervention group were significantly less likely to have provided a urine sample that contained a metabolite of any illicit drug. In addition, anti-HCV antibody positive patients in the intervention group were significantly more likely to have been given advice on reducing alcohol consumption (Table 4).

Although not to statistically significant levels, greater proportions of patients in the intervention group had been screened for hepatitis B, had been immunised against hepatitis A and B and if anti-HCV antibody positive, greater proportions of patients in the intervention group had been tested for HCV-RNA, had attended a hepatology clinic, had a liver biopsy performed and had antiviral therapy initiated (Table 4).

## DISCUSSION

### *Summary of main findings*

The cluster randomised controlled trial demonstrated that a complex intervention consisting of the dissemination of recently published clinical guidelines, a liaison nurse to assist practices with clinical care of patients and patient education, and educational support tailored to the needs of individual practices resulted in a significant increase in hepatitis C screening among current or former injecting drug users attending general practice. We were unable to demonstrate an increase in referral of anti-HCV antibody positive patients for hepatology assessment.

The intervention was also associated with a significant increase in the number of anti-HCV antibody positive patients who received advice on reducing alcohol and a significant decrease in the number of patients who provided their GP with a urine sample containing metabolites of illicit drugs.

### *Strengths and limitations of the study*

Although the study predated its publication, the design and conduct of the trial was in accordance with the recommendations contained in a revised CONSORT statement concerning cluster randomised trials.[32]

In order to provide comparability between intervention and control groups, stratification of GPs occurred prior to randomisation. With a relatively small number of GPs eligible for randomisation, it was felt unrestricted allocation or complete randomisation could introduce imbalance between groups for key practice characteristics.

Potential bias was introduced by data being extracted from clinical records. As chart abstraction

**Table 4. Comparison of secondary outcome measured between intervention and control populations at study completion analysed at patient and cluster level.**

| Evidence of secondary outcome in clinical record | Intervention *n* (%) | Control *n* (%) | Odds ratio (95% CI)[a] | Adjusted odds ratio (95% CI)[b] | *P*-value | ICC (95% CI) |
|---|---|---|---|---|---|---|
| Among study population | *n* = 104 | *n* = 92 | | | | |
| Mortalities | 0 (0) | 0 (0) | NA | NA | NA | NA |
| Still prescribed methadone by GP | 99 (95) | 86 (94) | 1.38 (0.41–4.69) | 2.26 (0.70–7.29) | 0.16 | 0 (0–0.30) |
| Provided urine sample containing metabolite of any illicit drug | 24 (23) | 50 (54) | 0.25 (0.14–0.47) | 0.16 (0.05–0.50) | 0.003 | 0.18 (0–0.61) |
| Provided urine sample containing opiate metabolite | 8 (8) | 23 (25) | 0.25 (0.11–0.59) | 0.26 (0.06–1.15) | 0.07 | 0.10 (0–0.36) |
| Tested for anti-HIV antibody by GP | 42 (40) | 31 (34) | 1.33 (0.74–2.39) | 1.54 (0.68–3.50) | 0.28 | 0.00 (0–0.3) |
| Tested for anti-HBc antibody or HBSag by GP | 51 (49) | 24 (26) | 2.73 (1.49–4.99) | 3.87 (1.28–11.66) | 0.02 | 0.10 (0–0.36) |
| At least one hepatitis B vaccine administered | 73 (70) | 38 (41) | 3.35 (1.85–6.04) | 4.66 (1.33–16.32) | 0.02 | 0.15 (0–0.52) |
| Complete course of hepatitis B vaccine administered | 37 (36) | 17 (19) | 2.44 (1.26–4.72) | 3.07 (0.94–10.01) | 0.06 | 0.06 (0–0.25) |
| At least one HAV vaccine administered | 40 (39) | 11 (12) | 4.60 (2.19–9.68) | 6.22 (1.36–28.52) | 0.02 | 0.16 (0–0.55) |
| Complete course of HAV vaccine administered | 11 (11) | 2 (2) | 5.32 (1.15–24.69) | 4.86 (0.76–31.10) | 0.09 | 0.05 (0–0.19) |
| Among patients who were anti-HCV positive | *n* = 73 | *n* = 41 | | | | |
| Advised on reducing alcohol | 49 (67) | 6 (15) | 11.91 (4.41–32.19) | 12.27 (2.70–55.76) | 0.003 | 0.41 (0–1.11) |
| Tested for the presence of HCV-RNA in serum | 41 (56) | 9 (22) | 4.56 (1.90–10.90) | 4.53 (1.02–20.14) | 0.05 | 0.20 (0–0.67) |
| Attended hepatology clinic | 37 (51) | 9 (22) | 3.65 (1.5–8.7) | 5.13 (1.1–23.1) | 0.04 | 0.14 (0–0.5) |
| Liver biopsy performed | 18 (25) | 3 (7) | 4.15 (1.14–15.06) | 5.07 (1.01–25.34) | 0.05 | 0.08 (0–0.32) |
| Antiviral therapy initiated | 5 (7) | 1 (3) | 2.94 (0.33–26.08) | 4.72 (0.42–53.23) | 0.20 | 0.00 (0–0.5) |

[a]*Patient level analysis.* [b]*Cluster level analysis.*

has recently been shown to underestimate quality of care for common outpatient general medical conditions when compared with standardised-patient reports,[34] it is possible the findings may have under-reported the true process of care delivered. However, the principal investigator reviewed a 10% random sample of clinical records from which the researcher had collected data and no inter-observer variation was noted. In addition, with data on both intervention and control populations being collected in an identical manner by the same researcher, data on both populations were subject to the same potential bias.

As a result, it was to be expected that no material differences between patients attending intervention and control practices would be identified at baseline. While both populations were comparable, in particular for the primary outcomes, the intervention group contained a higher proportion of males, thereby compromising internal validity. However, the inclusion of gender as a factor in subsequent multivariate logistic regression analysis is likely to have minimised any potential resulting bias.

External validity may have been compromised by selection bias at practice and individual patient level. Practices with fewer than eight patients on methadone at recruitment and practices where one of the GP principals was involved in developing or reviewing the clinical guidelines were excluded from this study. As a result, it is likely patients attending practices with limited experience or practices with extensive experience of caring for current or former drug users were not represented in this study. It is possible that the exclusion of less experienced GPs may have led to an underestimate of the effect of the intervention.

Nonetheless the sample of GPs was representative of all GPs in the region prescribing methadone at the time of the study in terms of the level of training in providing addiction related care and the health board area in which their practice was located.

Furthermore, while the study was limited to only one of Ireland's eight health regions, the most recently published data estimate that 85% of all people attending addiction treatment services in Ireland do so in this area.[19]

The systematic random sampling of patients was not feasible because of considerable variation in the maintenance of disease registers among the sample of participating practices. To minimise inter practice variations in sampling, therefore, a standardised non-probability sampling framework was used in which participating GPs sought consent from eight consecutive patients attending their practice for methadone maintenance treatment to allow his or her records be reviewed by a member of the research team. As GPs knew to which arm of the study they had been assigned and knew the patients who had consented to a member of the research team have access to their records, this may also have added to the selection bias.

Despite the potential bias introduced by these factors, the sample of patients on whom data is presented is similar in demographic and drug using characteristics to other larger samples of current or former injecting drug users in Ireland.[35,36]

### *Comparison with existing literature*

The role of general practice in the primary and secondary prevention of hepatitis C-related illness has recently been highlighted.[10] The clinical guidelines whose content formed the basis of this trial offered clear advice in this regard for GPs involved in the care of current or former injecting drug users and included harm reduction, immunisation against other hepatotrophic viruses and screening for hepatitis C (and other bloodborne viruses). In addition, for those patients who test anti-HCV antibody positive, they recommended lifestyle advice, diagnostic tests and referral for specialist assessment. Considerable overlap exists between these and other recent publications.[11,14]

By demonstrating a significant increase in screening for hepatitis C, the trial was in part successful. It is perhaps worth reflecting that at study completion, 25 people in the control group (compared to 24 at baseline) had been screened for hepatitis C. This finding is consistent with previous studies from Ireland, indicates a need for interventions that improve access to and uptake of screening for hepatitis C and supports the view that effective implementation of clinical guidelines requires adopting multi-faceted complex interventions that target individual barriers to change.[15,16]

While it is inappropriate to attempt to identify the elements of the complex intervention that were most important, some insights in this regard may be gained by our qualitative interviews with a representative sample of GPs to inform the design of the complex intervention conducted in advance of its introduction. These interviews highlighted the importance of clinical and organisational support to the successful implementation of the clinical guidelines and the potential contribution of a liaison nurse in this respect.[22]

These interviews also indicated the resource implications for primary care of effective guidelines implementation as lack of resources at practice level and lack of time were among the main barriers to effective implementation of the clinical guidelines. In the complex intervention, screening for hepatitis C was accompanied by information, advice, consent and support before and after testing, an approach whose importance has recently been highlighted.[37] Clearly while this approach should be incorporated in any subsequent intervention designed to improve screening for hepatitis C in primary care, it is likely to have considerable resource implications for primary care. It would appear that the resource implications of improving screening for hepatitis C, allied to the findings of this trial, justify the provision of such supports.

The trial did not demonstrate a significant increase in referral of anti-HCV antibody patients for assessment. This may be explained by the duration of the trial being too short as referring a patient for assessment represents a later stage in the care pathway. Alternatively, it may be explained by this outcome being subject to a larger clustering effect, (ICC = 0.13, compared to 0.09 in the case of screening for hepatitis C).

The finding that patients in the intervention group were less likely to provide a urine sample containing an illicit drug metabolite was unexpected, but welcome. This data had been collected to determine the extent to which screening and treating patients for bloodborne viruses would lead to relapse to illicit drug use and while the findings do not establish a causal link between the complex intervention and a reduction in illicit drug use, an association clearly exists. Once again, the additional time and care provided to patients in the intervention group by the liaison nurse should be considered as important in contributing to this outcome.

### *Implications for clinical practice and future research*

*Hepatitis C — an Action Plan for England*, has outlined the need for 'intensified action … to prevent

new infections, to reduce the level of undiagnosed infection and to provide better more coordinated pathways of care for people with hepatitis C, from their initial diagnosis to specialist care and treatment, if appropriate'.[38] While providing care that is informed by scientific evidence and expert consensus may be challenging, this study has demonstrated that when adequately supported by a complex (educational and clinical) intervention, general practice has an important role in caring for people at risk of or infected with hepatitis C, specifically the primary and secondary prevention of harm resulting from related illness.

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### Ethics committee

Irish College of General Practitioners (26/2/2001)

### Competing interests

The authors have stated that there are none

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